DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
m2701n

Chicago District
300 S. Riverside Plaza, Suite 550 South
Chicago, Illinois 60606
Telephone: 312-353-5863

May 25, 1999

WARNING LETTER
CHI-17-99

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Brian A. Tambi, President/CEO
Morton Grove Pharmaceuticals, Inc.
6451 W. Main Street
Morton Grove, IL 60053

Dear Mr. Tambi:

During an inspection of your drug manufacturing facility located at the above address, conducted from March 3, 1999, through April 12, 1999, FDA Investigators Yvonne Lozano and Nicholas Lyons found serious deviations from the current Good Manufacturing Practice Regulations (cGMP) (Title 21, Code of Federal Regulations, Parts 210 and 211). These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) as follows:

- Failure to reject drug products that failed to meet established specifications as required by 21 CFR 211.165(d). For example, [redacted] lots of Nystatin Oral Suspension USP exceeded the established upper specification for total aerobic count, but were released into commercial distribution based on retest results which were not conducted in conformance with established procedures.

- Failure to clean equipment, as appropriate, to prevent contamination of drug products and failure to establish sufficiently detailed equipment cleaning procedures as required by 21 CFR 211.67. For example:

  a. Diphen AF, lot 21906, was found to be contaminated with Promethazine HCl, which product was filled using the same equipment, on the same filling line, the previous day.
  b. Hyoscyamine Oral Drops, lot 21871, was found to be contaminated with Carbinoxamine Oral Drops, which product was filled on the same filling line the previous day, utilizing a common anchoring mechanism.
  c. Cleaning studies do not address microbial contamination issues.

- Failure to establish sufficient procedures to control microbiological contamination in the production of Nystatin Oral Suspension USP (21 CFR 211.113) as evidenced by the [redacted] lots of Nystatin Oral Suspension USP which exceeded the established upper specification for total aerobic count. The identity of the isolate was established as Acinetobacter baumanii.

- Failure to follow written sampling and testing plans as required by 211.165(c). For example, the retesting method used for the [redacted] lots of Nystatin that initially exceeded your specification for aerobic microbial count of [redacted] cfu/mL did not follow your established written procedure for retesting.

- Failure to have sufficient production and process controls to assure that drug products have the identity, strength, quality, and purity they purport or are represented to possess, i.e. a validated process, as required by 21 CFR 211.100. For example:

  a. Several lots of Selenium Sulfide Lotion, USP 2.5%, and a lot of Triamcinolone Acetonide Lotion, USP 1.0%, failed to meet finished product acceptance criteria.
  b. Failure to establish sufficient filling controls as evidenced by the rejection of one [redacted] skids of Mytex, lot 21714, and the rejection of a portion of Erythromycin Topical Solution, USP 2%, Lot 22159, as documented by your own failure investigation.

- Failure to conduct and/or fully document a thorough investigation of an unexplained discrepancy or the failure of a batch to meet its specifications as required by 21 CFR 211.192. For example:

  a. The origin of Acinetobacter baumanii found in both Lactulose solution and [redacted] lots of Nystatin Oral Suspension USP has not been determined.
  b. The origin of the "yellow" tint in Erythromycin Topical Solution, USP 2%, Lot 22159, was not determined.
  c. Stability failure investigations for: Triple Tannate Pediatric Suspension, lot numbers 21094 and 21216; Antispasmodic Elixir, lot 21614; and Pseudoephedrine HCl Syrup, lot 21377 (subsequently recalled), were incomplete.
  d. Failure investigations for Triamcinolone Acetonide Lotion, USP 0.025%, lot 21723, and Triamcinolone Acetonide Lotion, USP 0.1%, lot 21700, were incomplete.

- Failure to maintain equipment cleaning log/records as required. For example, not all equipment (mixers and bulk pumps) associated with the manufacture of Nystatin Oral Suspension had equipment cleaning and use logs/records completed. [21 CFR 211.67 and 211.182]

- Failure to accurately record fill volume/weight/torque measurements as required. During the filling of Nystatin Oral Suspension, the hourly checks done by the production employees were not recorded on the "daily filling record" even though adjustments were made to the filling machine after the employees conducted the unrecorded checks. [21 CFR 211.188]

- Failure to specifically define, in writing, the responsibilities of the quality control unit as required. For example, your Investigation procedure, your procedure entitled "Out of Specification (OOS) Results Investigations", and SOP entitled "Definition of the Quality Control Unit" are not sufficiently detailed regarding responsibilities. [21 CFR 211.22(d)]

- Failure to follow established procedures as required by 21 CFR 211.100(b). Examples include:

  a. Out of Specification (OOS) Results Investigation SOP QC-102-27.
  b. Inspection and Disposition of Raw Materials SOP QO-101-70.
  c. Handling of cGMP Complaint RA600-55.

We have reviewed your response dated May 5, 1999, which was written in response to the FDA-483 issued on April 12, 1999, and have the following comments.

Your response does not indicate what you intend to do regarding the products introduced into commercial distribution which contained the objectionable organism, Acinetobacter baumanii.

SOP QO-101-90/Rev. 3 states "All out of specification conditions may not result in a formal investigation. The Director of Quality Assurance or designate may determine that a written explanation may be satisfactory without having to open a formal investigation." However, there are no details included specifying when that would be appropriate, how that would be determined, or the conditions to be met.

Several responses can only be fully evaluated at a follow-up reinspection during which the newly established procedures can be adequately challenged, and process/cleaning validation data can be evaluated.

The above list of violations is not intended to be an all-inclusive list of deficiencies at your firm. It is your responsibility to ensure that all of your firm's products are in compliance with all requirements of the Act and its implementing regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunctions.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which corrections will be completed. Your response should be addressed to: Richard Harrison, Compliance Director, at the address provided in the letterhead.

Sincerely,

/s/
Raymond V. Mlecko
District Director

cc: Mr. Louis E. Windecker, P.Ph.
Executive Vice President
Morton Grove Pharmaceuticals, Inc.
6451 W. Main Street
Morton Grove, IL 60053

cc: Sanjeev Bahl, Director, Quality Assurance
Vice President/Regulatory Affairs
Morton Grove Pharmaceuticals, Inc.
6451 W. Main Street
Morton Grove, IL 60053